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10/529,203	03/25/2005	Horst Bauer	268034US0PCT	4774

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EXAMINER
HA, JULIE

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/529,203	BAUER ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8-14,16-18,20-22,25-27 and 29-60* is/are pending in the application.

4a) Of the above claim(s) *3, 5, 50-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,8-14,16-18,20-22,25-27,29-49 and 55-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment after Non-final rejection filed on September 11, 2007 is acknowledged. Claims 6-7, 15, 19, 23-24 and 28 have been canceled. Claims 1-5, 8-14, 16-18, 20-22 25-27 and 29-60 are pending in this application. Applicant elected with traverse Group I, drawn to a pharmaceutical gel preparation, a method for producing a pharmaceutical preparation and a method for treating a patient with a pharmaceutically active peptide compound and the election of species of D-63135 as the ionic peptide compound, GnRH antagonist, and sodium chloride as the inorganic salt. The restriction requirement was deemed proper and made FINAL in the previous office action. Claim 54 was withdrawn from further consideration, as being drawn to a nonelected invention. Claims 3, 5 and 50-53 were withdrawn from further consideration, as being drawn to non-elected species. Since the elected species appear to be a monovalent cationic peptide and a GnRH antagonist, claims 3 and 5 were withdrawn. Claims 1-2, 4, 8-14, 16-18, 20-22, 25-27, 29-49 and 55-60 are examined on the merits in this office action.

Withdrawn Objections

1. Objection to title is withdrawn due to Applicant's arguments.

2. Objection to specification is withdrawn due to Applicant's amendments to the specification.

Maintained Rejections

35 U.S.C. 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-2, 4, 8-10, 12-14, 16-18, 27, 33, 36-37, 43-49, 55-57 are rejected under 35 U.S.C. 102(b) as being anticipated by Gefter et al (US Patent # 6180608).

5. The instant claims are drawn to a method for producing a pharmaceutical preparation comprising the steps a) bringing together an amount of at least one pharmaceutically active peptide compound in lyophilized form and an aqueous solution of an inorganic or acetic acid salt and b) mixing the components. The claims are further drawn to step of sterilization of the peptide formulation by irradiation with gamma rays or electron beams.

6. As described in the previous office action, Gefter et al teach pharmaceutical compositions comprising a stable water-insoluble complex composed of a peptidic compound, preferably a pharmaceutically active peptidic compound, and a carrier macromolecule that allows for sustained delivery of the peptidic compound in vivo upon administration of the complex. The reference further teaches that the complex can permit continuous delivery of a pharmaceutically active peptidic compound to a subject for prolonged periods of time, e.g., one month, two months, three months and the like (see column 1, lines 43-52 and column 6, lines 12-13). This reads on claims 1, 33 and

44-47. Claims 44-47 and 55-57 do not recite further structural attributes that results in the sustained pharmaceutical activity for at least 12 weeks and colloidal dispersion and changes in its viscosity as function of time, respectively . The prior art discloses same peptide composition, therefore the sustained pharmaceutical activity and colloidal dispersion and its viscosity are inherent properties of the peptide. Thus, this meets the limitations of claims 44-47 and 55-57. Furthermore, the reference teaches that the complex is formed by combining the peptidic compound and the carrier macromolecule under conditions such that a substantially water-insoluble complex is formed, e.g., aqueous solutions of the peptidic compound and carrier macromolecule are mixed until the complex precipitates. The complex may be in the form of a solid (e.g., a paste, granules, a powder or a lyophilisate)...can be pulverized finely enough to form stable liquid suspensions or semi-solid dispersions (see column 1, lines 57-65). This reads on claim 33 and claim 36 in part. The reference further teaches that the peptidic compound of the water-insoluble complex is an LHRH analog, and LHRH antagonist (see column 1, lines 66-67 and column 2, line 1). Furthermore, the reference teaches that the complex is suitable for sterilization, such as by gamma irradiation or electron beam irradiation, prior to administration in vivo (see column 2, lines 3-5). This reads on claims 36 and 37. Further, the reference teaches a method for treating a subject for a condition (prostate cancer) treatable with an LHRH analog by administering to the subject an LHRH-analog-containing composition (see column 2, lines 6-11). This reads on claims 48-49. The LHRH analogs are LHRH antagonists, and include antide, Cetrorelix and the like (see column 4. lines 6-27). This reads on claims 8-10. The reference further

discloses that multivalent cationic peptidic compound and multivalent anionic peptidic compound refer to peptidic compound comprising a multiplicity of positive or negative charges (see column 3, lines 46-49). This reads on claims 2 and 4. Furthermore, the reference teaches that the pharmaceutical formulations comprise additional pharmaceutically acceptable carriers and/or excipients...the carrier is suitable for intravenous, intramuscular, subcutaneous or parenteral administration (e.g., by injection) (see column 7, lines 65-67 and column 8, lines 1-7). This reads on claim 43. The reference further teaches that a non-,limiting range of an LHRH analog is 0.01 mg to 10 mg/kg (see column 10. lines37-38) and Examples 2-4 discloses 25 mg of peptidic compound dissolved in water (Example 2), 50 mg of peptidic compound dissolved in mannitol and catboxymethylcellulose (Example 3) and 25 mg of peptidic compound dissolved in water and added to sodium alginate (Example 4). This reads on claims 16-18. The reference further teaches that the reconstitution vehicle to be used in clinical studies is 0.9% sodium chloride (see Example 14). This reads on claims 1, 12-14 and 27. Therefore, the prior art meets the limitations of claims 1-2, 4, 8-10, 12-14, 16-18, 27, 33, 36-37, 43-49 and 55-57.

Response to Applicant's Arguments

7. Applicant argues that the present invention relates to a sustained release pharmaceutical administration form wherein the pharmacologically active peptide is obtained by reconstituting a lyophilized peptide compound with a low-concentration of an inorganic or acetic acid salt solution before administration. Further, Applicant argues

that Gefter et al disclose a pharmaceutical composition comprising a water-insoluble complex composed of a peptidic compound and a macromolecule carrier that allows for sustained release of the peptidic compound and a macromolecule carrier that allows for sustained release of the peptidic compound in vivo upon administration of the complex. Further, Gefter et al teach LHRH analogs which may be an LHRH agonist or antagonist. Gefter et al does not disclose or suggest D-63153 or the concentration of sodium chloride. Gefter et al use a 0.9% sodium chloride in Example 14 as a reconstitution vehicle to reconstitute the complex PPI-149-CMC, consisting of the peptidic compound PPI-149 and the macromolecule carboxymethylcellulose, wherein the complex PPI-149-CMC is already a sustained delivery complex. However, the present invention uses sodium chloride as an inorganic salt as the reconstitution medium and to prepare a sustained release form from an easily soluble peptide or peptide salt, and peptide forms the administration form for sustained release itself.

8. Applicant's arguments have been considered but have not been found persuasive because Gefter et al teach a pharmaceutical composition comprising the peptidic compound PPI-149 and a macromolecule for sustained release and this composition is reconstituted in 0.9% sodium chloride as claimed. Gefter et al further teaches that PPI-149 has the peptide sequence Ac-D-Nal^{1}-4-Cl-D-Phe^{2}-D-Pal^{3}-N-Me-Tyr^{5}-D-Asn^{6}-Lys(iPr)^{8}-D-Ala^{10}-LHRH, which is an LHRH antagonist (see claim 11). The composition of the Gefter patent is being reconstituted in the same concentration of sodium salt, and since the claimed invention of instant application is drawn to a pharmaceutical gel preparation comprising a mixture of (a) at least one

pharmaceutically active ionic peptide compound having from 8 to 12 amino acids in lyophilized form, and (b) an aqueous solution of an inorganic or acetic acid at a concentration from 0.01% to about 0.9% (weight/volume), and there are no other structural limitations from the base claim, the prior art meets the limitation of the base claim. It is inconsequential that Gefter composition comprises a macromolecule, since the only structural limitation of instant claimed invention is that the peptide compound has a length of from 8 to 12 amino acids in lyophilized form, and Gefter patent teaches a peptide that meets this limitation, since LHRH is a decapeptide, and PPI-149 has the sequence Ac-D-Nal^{1}-4-Cl-D-Phe^{2}-D-Pal^{3}-N-Me-Tyr^{5}-D-Asn^{6}-Lys(iPr)^{8}-D-Ala^{10}-LHRH. Therefore the reference meets the limitations of claims 1-2, 4, 8-10, 12-14, 16-18, 27, 33, 36-37, 43-49 and 55-57.

Rejection-35 U.S.C. 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 11, 20-22, 25-26, 29-32 and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gefter et al (US Patent # 6180608) as applied to claims 1-2, 4, 8-10, 12-14, 16-18, 27, 33, 36-37, 43-49 and 55-57 above, and further in view of Bauer et al (PG Pub 2002/039996).

13. The instant claims are drawn to a pharmaceutical preparation wherein the pharmaceutically active ionic peptide compound is the GnRH antagonist D-63153 in an amount of about 5 to about 50 mg per ml of the total amount of the pharmaceutical preparation, and the NaCl is from about 0.05% to about 0.5% (W/V) and the production of the peptide formulation takes place with use of aseptic procedures.

14. The teachings of Gefter et al are described supra, the difference between the reference and the instant claims are that the reference does not teach D-63153 and differing NaCl concentrations.

15. However, Bauer et al disclose a pharmaceutical administration forms suitable for parenteral administration, which contains peptides prone to aggregation in the form of their acetate, gluconate, glucuronate, lactate, citrate, ascorbate, benzoate, or phosphate salts in dissolved or dispersed form (see abstract). Furthermore, the reference discloses that the pharmaceutical administration forms can be present in dissolved or dispersed form in water or in aqueous solvent mixtures (see paragraph [0012]). Additionally, the reference discloses that the peptides employed are LHRH antagonists antide, A-75998, ganirelix and Nal-Glu antagonist, but in particular cetrorelix, antarelix and the antagonists according to the U.S. Patent # 5942493 and DE 19911771.3. (see paragraph [0014] and US Patent # 7005418, column 3, lines 53-58). D-63153 is an antagonist disclosed in DE 19911771.3. Furthermore, the reference discloses that preparation of sterile solutions of LHRH antagonist for parenteral administration is by means of filtration, especially at high concentration (see paragraph [0009]). Additionally, the reference discloses that the administration of pharmaceutically active peptides is the parenteral pharmaceutical form...in the form of reconstituted lyophilisates of soluble peptide salts and to microparticles, microcapsules or implants (see paragraph [0010]). Furthermore, the reference discloses that area of use of the preparations is in the prevention and therapy of all sex hormone-dependent conditions and diseases, which can be influenced by LHRH agonist and antagonists...benign prostate hyperplasia, carcinoma of the prostate, precocious puberty, hirsutism, endometrial hyperplasia, uterine myomatosis, breast cancer, etc (see paragraphs [0020] and [0021] and claims 16 and 17). Furthermore, the reference discloses rat animal experiment (see paragraph

[0041] and Tables 8a, 8b and 9). Please note that the reference discloses the disorders that are claimed in claims 50-53 of instant application.

16. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Gefter et al and Bauer et al because both prior arts teach pharmaceutical gel formulation incorporating GnRH antagonist. There is a motivation to substitute D-63153 for other GnRH antagonists since they are all recognized GnRH antagonist and one would expect the same activity. There is a reasonable expectation of success to substitute D-63153 for other GnRH antagonist, since both prior arts disclose Antide and Cetrorelix as examples of GnRH antagonists that can be formulated into composition in an aqueous solvent. Further, there is a reasonable expectation of success since 0.9% sodium chloride is used to reconstitute for clinical studies (see Example 14 of patent '608) and sustained delivery formulation for administering pharmaceutically active peptides in vivo continuously for prolonged time periods are achieved by patent '608. The references are silent as to the range of NaCl concentrations.

17. However, the MPEP states the following: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. *"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."* In re Aller, *220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)* (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration

between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"); *In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969)* (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Therefore, there is a reasonable expectation of success to optimize the NaCl concentration, since "*The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.*"

Response to Applicant's Arguments

18. Applicant argues that Bauer et al discloses that peptides have a nature to prone to uncontrolled aggregation and that the peptides if administered lead to a

concentration-dependent lowering of the bioavailability from the peptide concentration. Addition of free acid to the easily soluble peptide salt prevents that peptide salts prone to aggregation, thus with deficiencies of Gefter stated previously, and Bauer et al do not lead to the inventive subject matter.

19. Applicant's arguments have been considered but have not been found persuasive, since Bauer reference teaches that pharmaceutically active decapeptides (cetrorelix) in the form of their pharmaceutically acceptable, non-toxic acid addition salts such as hydrochlorides...acetates, citrates...etc (see paragraph [0002]). Further, the reference discloses pharmaceutical administration forms suitable for parenteral administration, which contains peptides prone to aggregation in dissolved or dispersed form and the peptides are present in the form of their acetate salts. Further, the reference discloses that the administration of pharmaceutically active peptides is the parenteral pharmaceutical form...in the form of reconstituted lyophilisates of soluble peptide salts and to microparticles, microcapsules or implants (see paragraph [0010]). Furthermore, the reference discloses that area of use of the preparations is in the prevention and therapy of all sex hormone-dependent conditions and diseases. Furthermore, both prior arts teach pharmaceutical gel formulation incorporating GnRH antagonist. There is a motivation to substitute D-63153 for other GnRH antagonists since they are all recognized GnRH antagonist and one would expect the same activity. Since the claims do not further limit the structural attributes of the pharmaceutical gel preparation except the peptides have lengths of from 8 to 12 amino acids and since the prior arts teach the peptides having these limitations in pharmaceutical gel preparations,

the prior arts meet the limitations of claims 11, 20-22, 25-26, 29-32 and 34-35 as well as claims 1-2, 4, 8-10, 12-14, 16-18, 27, 33, 36-37, 43-49 and 55-57.

20. Claims 38-42 and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gefter et al (US Patent #6180608) in view of Bauer et al (PG Pub 2002/039996) as applied to claims 1-2, 4, 8-14, 16-8, 20-22, 25-27, 29-33, 34-37, 43-49 and 55-57 above, and further in view of Engel et al (US Patent # 5663145).

21. The instant claims are drawn to a kit for producing a pharmaceutical preparation, comprising a pharmaceutically active D-63153 (about 25 mg) in lyophilized form and of an aqueous solution of an inorganic or acetic acid salt, mannitol, and sodium chloride in about 0.1% weight/volume.

22. As described supra, Gefter et al and Bauer et al teach pharmaceutical formulation comprising GnRH antagonist in aqueous form. The difference between the references and the instant claims is that the references do not teach a kit.

23. However, Engel et al teach substances available for treating hormone-dependent malignant diseases (see column 1, lines 6-7). Further, the reference teaches that Cetrorelix (INN) is an antagonist for LHRH (see column 1, line 15). The reference discloses that in clinical trials, a daily dose of 10 mg showed a complete suppression of the hormone concentration to castration level (see column 1, lines 20-22). Additionally, the reference discloses the dosage regimen of the pharmaceutical composition: an initial dose with the amount of 1-60 mg in a lyophilisate ampoule or several lyophilisate ampoules; lyophilisate ampoules in a slow-release form with a rate of delivery of 0.1-10 mg/day for the whole period of treatment; or lyophilisate ampoules which contain the

amount of active substance, which is not in a slow-release form, in an amount of 0.1-10 mg (see column 1, lines 42-54). The reference further teaches the aseptic procedures and lyophilizing the Cetrorelix solution (see column 2, lines 24-40). Furthermore, the reference teaches a kit comprising LHRH antagonist, Cetrorelix (see claims 1-3) and the method of treating a hormone-dependent condition (prostate cancer) comprising administering LHRH antagonist (Cetrorelix) (see claims 7 and 13).

24. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Gefter and Bauer and Engel because the prior arts teach the pharmaceutical formulation of GnRH antagonists in liquid form. All three prior arts teach the method of treating a hormone-dependent condition (prostate cancer) by administering a pharmaceutical composition of Cetrorelix. Bauer further discloses D-63153 as one of the peptides employed (see paragraph [0014] and see US Patent # 7005418, column 3, lines 53-58). One of ordinary skill in the art would be motivated to substitute D-63153 for other GnRH antagonists since they are all recognized GnRH antagonist according to the prior arts, and thus, one would expect the same activity. There is a reasonable expectation of success since the Bauer and Engel teach the use of the formulation for the treatment of hormone-dependent disorder, specifically prostate cancer. Furthermore, there is a reasonable expectation of success since GnRH antagonists have similar properties, such as solubility, and are used to treat the same disorders.

Response to Applicant's Arguments

25. Applicant argues that Engel et al teach a kit comprising an initial dose of an LHRH antagonist and at least one maintenance does of the same LHRH antagonist for the treatment of hormone-dependent conditions. The current invention claims related to a kit comprising an LHRH antagonist as finished preparation of the peptide compound and a solution of an inorganic salt or acetic acid salt for reconstitution. The combination of teaching of Gefter et al, Bauer et al, and of Engel et al does not lead to the inventive subject matter of the kit claimed.

26. Applicant's arguments have been considered but have not been found persuasive because all three cited prior arts teach the pharmaceutical formulation of GnRH antagonists in liquid form. Furthermore, Gefter et al teaches that the GnRH (LHRH) antagonist is in solid form (lyophilisate) and reconstituted in NaCl for clinical purposes. All three prior arts teach the method of treating a hormone-dependent condition (prostate cancer) by administering a pharmaceutical composition of Cetrorelix. Bauer further discloses D-63153 as one of the peptides employed (see paragraph [0014] and see US Patent # 7005418, column 3, lines 53-58). Since the claims do not further limit the structural attributes of the pharmaceutical gel preparation, and Engel et al teach the dosage regimen: an initial dose with the amount of 1-60 mg in a lyophilisate ampoule or several lyophilisate ampoules; lyophilisate ampoules in a slow-release form with a rate of delivery of 0.1-10 mg/day for the whole period of treatment; or lyophilisate ampoules which contain the amount of active substance, which is not in a slow-release form, in an amount of 0.1-10 mg (see column 1, lines 42-54) and furthermore, teach a

kit comprising the LHRH antagonist. Since Engel et al teach the kit comprising dosage in lyophilisate ampoules (see claims 4-5) and in slow-releasing formulation (see claim 6), this meets the limitations of claim 48. Therefore, the prior arts combined meets the limitations of claims 38-42 and 58-60 and 1-2, 4, 8-14, 16-8, 20-22, 25-27, 29-33, 34-37, 43-49 and 55-57.

Conclusion

27. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). No claims are allowed.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Julie Ha
Patent Examiner
AU 1654

10/30/14
ANISH GUPTA
PRIMARY EXAMINER